

Safety Data Sheet (SDS) According to the REACH Regulation (EC) No. 1907/2006

Issuing Date: 2015-01-20

Revision Date: 2017-09-12

Version: 2

SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1. Product identifier

Product No	14703
Product name	Tofacitinib
Reach registration number	This substance/mixture contains only ingredients which have been registered, or are exempt from registration, according to Regulation (EC) No. 1907/2006.

Contains

Chemical Name	Index No.	CAS No
3-[(3R,4R)-4-methyl-3-[methyl(7H-pyrrolo[2,3-d]p yrimidin-4-yl)amino]piperidin-1-yl]-3-oxopropaneni trile (90 - 100%)	Not Listed	477600-75-2

Formula	C ₁₆ H ₂₀ N ₆ O
Molecular Weight	312.37 g/mol
Other means of identification	14703L, 14703M, 14703S

1.2. Relevant identified uses of the substance or mixture and uses advised against

Identified uses	For research use only
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1.3. Details of the supplier of the safety data sheet

Importer (Applicable in EU only)	Manufacturer
Cell Signaling Technology Europe B.V. Schuttersveld 2 2316 ZA Leiden The Netherlands TEL: +31 (0)71 7200 200 FAX: +31 (0)71 891 0098	Cell Signaling Technology, Inc. 3 Trask Lane Danvers, MA 01923 United States TEL: +1 978 867 2300 FAX: +1 978 867 2400

Website	www.cellsignal.com
E-mail Address	info@cellsignal.eu

1.4. Emergency telephone number

CHEMTREC 24 hours a day, 7 days a week, 365 days a year
+1 703 527 3887 (INTERNATIONAL) +1 800 424 9300 (NORTH AMERICA)

Europe	112
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SECTION 2: Hazards identification

2.1. Classification of the substance or mixture

Regulation (EC) No. 1272/2008

Carcinogenicity	Category 2 - (H351)
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Reproductive toxicity	Category 1B - (H360Df)
Specific target organ toxicity - repeated exposure (STOT RE)	Category 2 - (H373)

For the full text of the H-phrases & EUH-phrases mentioned in this Section, see Section 16

2.2. Label elements



Signal word

Danger

Hazard statement(s)

H351 - Suspected of causing cancer if swallowed

H360Df - May damage the unborn child. Suspected of damaging fertility

H373 - May cause damage to organs through prolonged or repeated exposure if swallowed

Precautionary statement(s)

P201 - Obtain special instructions before use

P202 - Do not handle until all safety precautions have been read and understood

P260 - Do not breathe dust/fume/gas/mist/vapors/spray

P281 - Use personal protective equipment as required

P308 + P313 - IF exposed or concerned: Get medical advice/attention

P501 - Dispose of contents/container to an approved waste disposal plant

2.3. Other hazards

None under normal use conditions.

SECTION 3: Composition/information on ingredients

3.1 Substances

Synonyms

Tasocitinib;
CP-690550; 3-Piperidinamine,
1-(cyanoacetyl)-4-methyl-N-methyl-N-1H-pyrrolo(2,3-d)pyrimidin-4-yl-, (3R,4R)-

Formula

C₁₆H₂₀N₆O

Chemical nature

Monoconstituent substance.

Chemical Name	CAS No	Weight %	EC No	Classification (1272/2008)	REACH Registration Number
3-[(3R,4R)-4-methyl-3-[methyl(7H-pyrrolo[2,3-d]pyrimidin-4-yl)amino]piperidin-1-yl]-3-oxopropanenitrile	477600-75-2	100	-	Carc. 2 (H351) Repr. 1B (H360Df) STOT RE 2 (H373)	no data available

For the full text of the R-phrases mentioned in this Section, see Section 16

SECTION 4: First aid measures

4.1. Description of first aid measures

General advice	Immediate medical attention is required. Show this safety data sheet to the doctor in attendance.
Inhalation	Immediate medical attention is required. Move to fresh air. If not breathing, give artificial respiration.
Skin contact	Immediate medical attention is required. Wash off immediately with soap and plenty of water removing all contaminated clothes and shoes.
Eye contact	Rinse thoroughly with plenty of water, also under the eyelids. Keep eye wide open while rinsing.
Ingestion	Do NOT induce vomiting. Immediate medical attention is required. Never give anything by mouth to an unconscious person. Drink plenty of water.
Protection of first-aiders	Use personal protective equipment. Avoid contact with skin, eyes and clothing.

4.2. Most important symptoms and effects, both acute and delayed

Upper respiratory tract infections (common cold, sinus infections), headache, diarrhea, nasal congestion, sore throat, and runny nose (nasopharyngitis).

4.3. Indication of any immediate medical attention and special treatment needed

Notes to physician Treat symptomatically.

SECTION 5: Firefighting measures

5.1. Extinguishing media

Suitable Extinguishing Media	Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
Unsuitable Extinguishing Media	No information available.

5.2. Special hazards arising from the substance or mixture

Thermal decomposition can lead to release of irritating gases and vapors.

5.3. Advice for firefighters

Wear self-contained breathing apparatus and protective suit. Use personal protective equipment.

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

For non-emergency personnel	Evacuate personnel to safe areas. Ensure adequate ventilation.
For emergency responders	Use personal protection recommended in Section 8.

6.2. Environmental precautions

Should not be released into the environment. Prevent further leakage or spillage if safe to do so. Local authorities should be advised if significant spillages cannot be contained.

6.3. Methods and material for containment and cleaning up

Methods for containment	Prevent further leakage or spillage if safe to do so.
Methods for cleaning up	Take up mechanically, placing in appropriate containers for disposal.

6.4. Reference to other sections

See Sections 8 & 13 for additional information.

SECTION 7: Handling and storage

7.1. Precautions for safe handling

When using, do not eat, drink or smoke. Provide regular cleaning of equipment, work area and clothing. Avoid contact with skin, eyes and clothing. Wash hands before breaks and immediately after handling the product. Keep away from food, drink and animal feeding stuffs.

7.2. Conditions for safe storage, including any incompatibilities

Keep container tightly closed in a dry and well-ventilated place.

7.3. Specific end use(s)

Use as a laboratory reagent.

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

8.2. Exposure controls

Appropriate engineering controls

Showers, eyewash stations, and ventilation systems.

Individual protection measures, such as personal protective equipment

Eye/face protection	Tightly fitting safety goggles.
Skin protection	
Hand protection	Impervious gloves.
Other	Impervious gloves. Impervious clothing.
Respiratory protection	In case of inadequate ventilation wear respiratory protection.

Environmental Exposure Controls

No information available.

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Physical state	Solid
Appearance	Crystalline Powder Granules
Color	White to off-white
Odor	No information available
Odor Threshold	No information available

<u>Property</u>	<u>Values</u>	<u>Remarks • Method</u>
pH		No information available
Melting point/freezing point		No information available
Initial boiling point and boiling range		No information available
Flash point		No information available.
Evaporation rate		No information available
Flammability (solid, gas)		No information available
Upper flammability limit		No information available
Lower flammability limit		No information available
Vapor pressure		No information available
Vapor density		No information available
Relative density		No information available
Solubility	Practically insoluble	

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Partition coefficient: n-octanol/water	No information available
Autoignition temperature	No information available
Decomposition temperature	No information available.
Viscosity	No information available
Explosive properties	No information available
Oxidizing properties	No information available

9.2. Other information

Softening point	No information available
Molecular Weight	312.37 g/mol
Solubility in other solvents	Soluble in dimethyl sulfoxide (DMSO) @ 100 mg/mL, Soluble in ethanol (EtOH) @ 100 mg/mL
VOC content	No information available
Density	No information available.

SECTION 10: Stability and reactivity

10.1. Reactivity

No information available.

10.2. Chemical stability

Stable under normal conditions.

10.3. Possibility of hazardous reactions

Hazardous polymerization	Hazardous polymerization does not occur.
Hazardous reactions	None under normal processing.

10.4. Conditions to avoid

None known based on information supplied.

10.5. Incompatible materials

No information available.

10.6. Hazardous decomposition products

None under normal use conditions.

SECTION 11: Toxicological information

11.1. Information on toxicological effects

This material should only be handled by, or under the close supervision of, those properly qualified in the handling and use of potentially hazardous chemicals. It should be borne in mind that the toxicological and physiological properties of this compound is not well defined.

Information on likely routes of exposure

Inhalation	May cause irritation of respiratory tract.
Eye contact	Contact with eyes may cause irritation.
Skin contact	May cause irritation.
Ingestion	May be harmful if swallowed. Reproductive Toxicity.
Symptoms	Upper respiratory tract infections (common cold, sinus infections), headache, diarrhea, nasal congestion, sore throat, and runny nose (nasopharyngitis).
Skin corrosion/irritation	No information available.

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Serious eye damage/eye irritation	No information available.
Sensitization	No information available.
Mutagenic effects	Tofacitinib was not mutagenic in the bacterial reverse mutation assay. It was positive for clastogenicity in the in vitro chromosome aberration assay with human lymphocytes in the presence of metabolic enzymes, but negative in the absence of metabolic enzymes. Tofacitinib was negative in the in vivo rat micronucleus assay and in the in vitro CHO-HGPRT assay and their in vivo rat hepatocyte unscheduled DNA synthesis assay.
Carcinogenic effects	In a 39-week toxicology study in monkeys, tofacitinib at doses of 5 mg/kg (oral) twice daily produced lymphomas. In a 24-month oral carcinogenicity study in Sprague-Dawley rats, tofacitinib caused benign Leydig cell tumors, hibernomas (malignancy of brown adipose tissue), and benign thymomas at doses greater than or equal to 30 mg/kg/day.
Reproductive toxicity	In a rat embryofetal developmental study, tofacitinib was teratogenic at 100 mg/kg/day. Teratogenic effects consisted of external and soft tissue malformations of anasarca and membranous ventricular septal defects, respectively, and skeletal malformations or variations (absent cervical arch; bent femur, fibula, humerus, radius, scapula, tibia, and ulna; sternoschisis; absent rib; misshapen femur; branched rib; fused rib; fused sternebra; and hemicentric thoracic centrum). No developmental toxicity was observed in rats at 30 mg/kg/day. In a rabbit embryofetal developmental study, tofacitinib was teratogenic at 30 mg/kg/day in the absence of signs of maternal toxicity. Teratogenic effects included thoracogastroschisis, omphalocele, membranous ventricular septal defects, and cranial/skeletal malformations (microstomia, microphthalmia), mid-line and tail defects. No developmental toxicity was observed in rabbits at 10 mg/kg/day.
STOT - single exposure	No information available.
STOT - repeated exposure	May cause disorder and damage to the: Lymphatic System, Blood.
Target Organ Effects	Lymphatic System, Blood, Reproductive system.
Aspiration Hazard	No information available.
Other information	No information available.

SECTION 12: Ecological information

12.1. Toxicity

No information available.

12.2. Persistence and degradability

Not readily biodegradable.

12.3. Bioaccumulative potential

Bioaccumulation	Not likely to bioaccumulate.
Bioconcentration factor (BCF)	No information available.

Chemical Name	Octanol-Water Partition Coefficient
3-[(3R,4R)-4-methyl-3-[methyl(7H-pyrrolo[2,3-d]pyrimidin-4-yl)amino]piperidin-1-yl]-3-oxopropanenitrile	1.808

12.4. Mobility in soil

Is not likely mobile in the environment due its low water solubility.

12.5. Results of PBT and vPvB assessment

No information available.

12.6. Other adverse effects

No information available

SECTION 13: Disposal considerations

13.1. Waste treatment methods

Waste from residues / unused products	Dispose of in accordance with local regulations.
Contaminated packaging	Empty containers should be taken to an approved waste handling site for recycling or disposal.
Other information	According to the European Waste Catalogue, Waste Codes are not product specific, but application specific. Waste codes should be assigned by the user based on the application for which the product was used.

SECTION 14: Transport information

IMDG/IMO

14.1 UN number	Not regulated
14.2 UN proper shipping name	Not regulated
14.3 Transport hazard class(es)	Not regulated
14.4 Packing group	Not regulated
14.5 Environmental hazards	None
14.6 Special precautions for user	None
14.7 Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code	Not regulated

ADR/RID

14.1 UN number	Not regulated
14.2 UN proper shipping name	Not regulated
14.3 Transport hazard class(es)	Not regulated
14.4 Packing group	Not regulated
14.5 Environmental hazards	None
14.6 Special precautions for user	None

IATA

14.1 UN number	Not regulated
14.2 UN proper shipping name	Not regulated
14.3 Transport hazard class(es)	Not regulated
14.4 Packing group	Not regulated
14.5 Environmental hazards	None
14.6 Special precautions for user	None

SECTION 15: Regulatory information

15.1. Safety, health and environmental regulations/legislation specific for the substance or mixture

Candidate List of Substances of Very High Concern for Authorization Information

This product does not contain Substances of Very High Concern (SVHC).

SEVESO Directive Information

This product does not contain substances identified in the SEVESO Directive.

International inventories

TSCA 8(b)	-
DSL/NDSL	-
EINECS/ELINCS	-
ENCS	-
IECSC	-
KECL	-
PICCS	-
AICS	-

International inventories legend

TSCA - United States Toxic Substances Control Act Section 8(b) Inventory

DSL/NDSL - Canadian Domestic Substances List/Non-Domestic Substances List

EINECS/ELINCS - European Inventory of Existing Commercial Chemical Substances/EU List of Notified Chemical Substances

ENCS - Japan Existing and New Chemical Substances

IECSC - China Inventory of Existing Chemical Substances

KECL - Korean Existing and Evaluated Chemical Substances

PICCS - Philippines Inventory of Chemicals and Chemical Substances

AICS - Australian Inventory of Chemical Substances

15.2. Chemical safety assessment

For this substance a chemical safety assessment has not been carried out

SECTION 16: Other information

Full text of H-Statements referred to under Sections 2 and 3

H351 - Suspected of causing cancer if swallowed

H360Df - May damage the unborn child. Suspected of damaging fertility

H373 - May cause damage to organs through prolonged or repeated exposure if swallowed

Classification procedure: Expert judgment and weight of evidence determination.

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Disclaimer

The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text.